Chapter 10

Semisolid Dosage Forms and Transdermal Systems

Taken From: Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems by Allen Jr., Popovich and Ansel

Amican | Ares | Ballester | Barcelona | Calleja
2DPh

Ointments

Ointments

- Semisolid preparations
- External application
- May be medicated or not
- Protectants, lubricants, emollients
- Ointment bases

Ointment bases by USP

Oleaginous
Absorption
Water removable
Water soluble

Oleaginous Bases

- **Hydrocarbon bases**
- **Emollient effect**
- **Occlusive dressings**
- **Difficult to wash off**

Oleaginous Bases

- **Water and aqueous preparations may be incorporated but only in small amounts with some difficulty.**
- **When powdered substances are to be incorporated into hydrocarbon bases, liquid petrolatum (mineral oil) may be used as levigating agent.**

Oleaginous Bases

EXAMPLES:

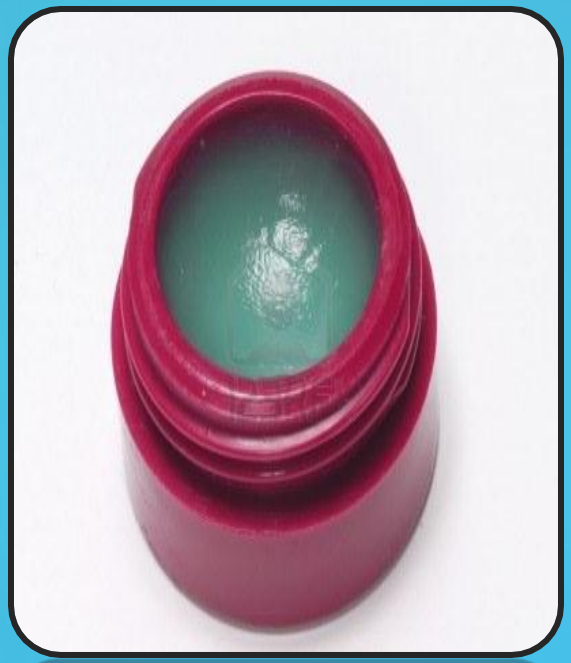
Petrolatum, USP

White Petrolatum, USP

Oleaginous Bases

EXAMPLES:

Yellow Ointment, USP



White Ointment, USP

Absorption Bases

- **Emollients, although they do not provide the degree of occlusion afforded by the oleaginous bases**
- **Not easily removed, external phase of the emulsion is oleaginous**
- **Pharmaceutical adjuncts to incorporate small volumes of aqueous solutions into hydrocarbon phases**

Absorption Bases

A. Those that permit the incorporation of aqueous solutions resulting in the formation of water in oil (W/O) emulsions

Absorption Bases

Examples:

Hydrophilic Petrolatum

Aquaphor, a variation of hydrophilic petrolatum, has the capacity to absorb up to 3x its weight in water and useful to incorporate a water-soluble drug, e.g. tobramycin sulfate , into a oleaginous ointment base. This concept is used in the preparation of ophthalmic ointments. Eucerin is a 50% W/O emulsion.

Absorption Bases

B. Those that are W/O emulsions that permit the incorporation of additional quantities of aqueous solutions

Absorption Bases

Examples:

Lanolin, USP

Water-Removable Bases

- Oil in water (O/W) emulsions, creams
- Water washable bases
- May be diluted
- Can absorb serous discharges

Water-Removable Bases

Examples

fougera®
NDC 0168-0047-16
Hydrophilic Ointment
(Differs from USP)
FOR EXTERNAL USE ONLY
AVOID CONTACT WITH EYES.
NET WT 453.6 g (1 lb)
E. FOUGERA & CO.
a division of Altana Inc.
MELVILLE, NEW YORK 11747
www.fougera.com
FOR USE AS AN OINTMENT OR COSMETIC BASE.
Keep this and all drugs out of the reach of children.
In case of accidental ingestion, seek professional assistance, or contact a Poison Control Center immediately.
R9/99

Hydrophilic Ointment, USP

Water-Soluble Bases

- Don't contain oleaginous components
- Completely water washable, greaseless
- Large amounts of aqueous solutions are not effectively incorporated into these bases
- Mostly used for incorporation of solid substances

Water-Soluble Bases

Example:

Polyethylene glycol (PEG) ointment, prototype example

Selection of Appropriate Base

Selection of the Appropriate Base

- **Desired release rate of the drug substance from the ointment base**
- **Desirability of topical or percutaneous drug absorption**
- **Desirability of occlusion of moisture from the skin**

Selection of the Appropriate Base

- **Stability of the drug in the ointment base**
- **Effect, if any, of the drug on the consistency or other features of the ointment base**
- **Desire for base easily removed by washing with water**
- **Characteristics of the surface to which it is applied**

Selection of the Appropriate Base

Example

- **Ointment is generally applied to dry, scaly skin**
- **Cream is applied to weeping or oozing surfaces**
- **Lotion is applied to intertriginous areas or where friction may occur, as between thighs or under the armpit**
- **The base which provides the best combination of the most desired attributes should be selected**

Preparation of Ointments

Incorporation

Fusion

*Depending primarily on the nature of the ingredients

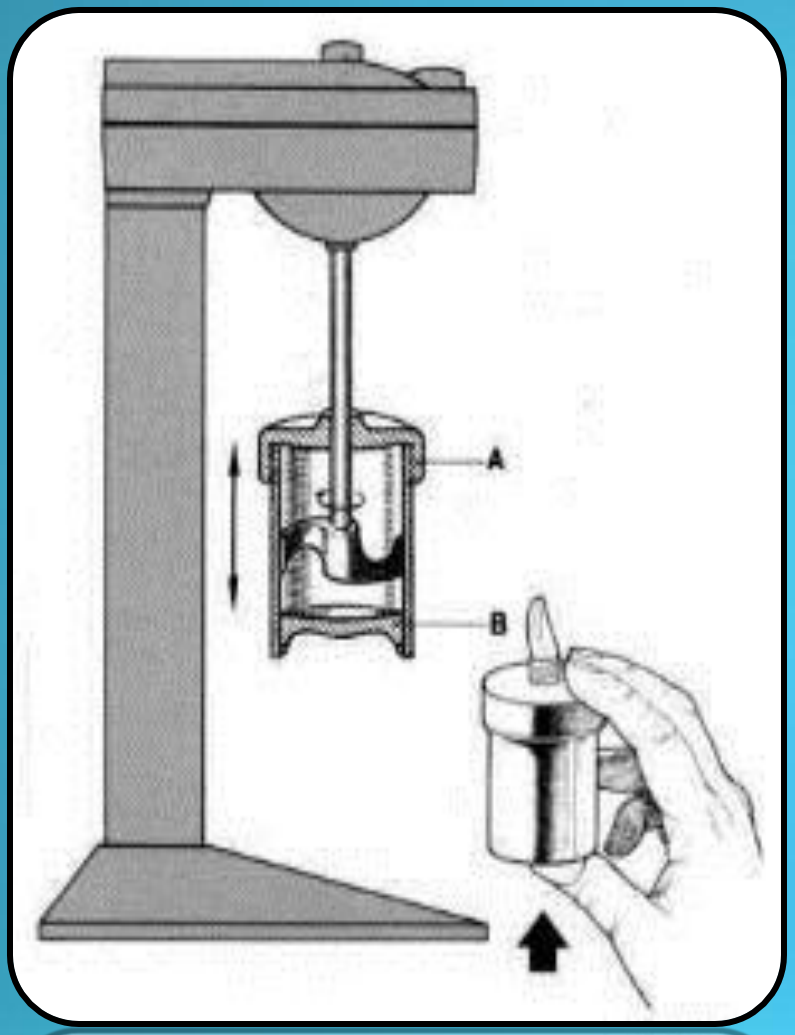
Incorporation

- **Components are mixed until a uniform preparation is attained**
  - Ointments and creams in batch sizes up to 1,500 kg are manufactured in stainless steel tank, which has a counter sweep agitation and a built-in homogenizer.

Incorporation

- **Mortar and pestle**
- **Spatula together with an ointment slab (large glass, porcelain plate, or pill tile)**
- **Ointment mill - an electronic mortar and pestle, "Unguator"**

Incorporation



Incorporation of Solids

- If the components of an ointment react with metal, hard rubber spatulas may be used.
- The ointment is prepared by thoroughly rubbing and working the components together on the hard surface until the product is smooth and uniform.
- Geometric dilution is used until all portions of the powder and base are combined thoroughly and uniformly blended.

Incorporation of Solids

- **It is often desirable to reduce the particle size of a powder or crystalline material before incorporation into the ointment, so it will not be gritty.**

Incorporation of Solids

- **Levigating –mixing the solid material in a vehicle in which it is insoluble to make smooth dispersion.**
  - **Levigating agent should be physically and chemically compatible with the drug and base**
    - **mineral oil for bases in which oils are the external phase**
    - **Glycerin for bases in which water is the external phase**

Incorporation of Solids

- **Solids soluble in a common solvent that will affect neither the stability of the drug nor the efficacy of the product may first be dissolved in that solvent (water or alcohol)**
- **The solution added to the ointment base by spatulation or mortar and pestle (preffered when large vol of liquids are added, because the liquid is more captive than on an ointment slab)**

Incorporation of Solids

For incorporating a gummy material, such as camphor

Incorporation of Solids

- **Pulverization by intervention**
  - **Material is dissolved in a solvent and spread out in a pill tile**
  - **The solvent is allowed to evaporate, leaving a thin film of the material onto which the other ingredient or ingredients are spread.**
  - **The material is then worked into the ingredients by trituration with a spatula.**

Incorporation of Liquids

- **Must put into consideration the ointment base's capacity to accept the volume required.**
  - **Oleaginous base (white petrolatum) – little amount of water**
  - **Hydrophilic Bases (PEG or Polyethylene Glycolor Macrogol) – Readily accept aqueous solutions**
    - **Absorption base, Emulsion Base, Water soluble base are HYDROPHILIC BASES**

  Note: All bases have their limits to retain liquids.

Adding liquid to a Hydrophobic Base

Add the liquid to a minimum amount of hydrophilic base

Add the mixture to the hydrophobic base

Incorporation of Liquids

- **Small volumes of Alcoholic liquids may easily be added to oleaginous vehicles or emulsion bases**
- **Natural Balsams (Peru Balsam) are to be mixed with an equal portion of castor oil before incorporation to a base.**
  - **This reduces the surface tension of the balsam**

***Ointment or roller mills maybe used to produce ointments uniform in composition and texture.**

DermaMill

Fusion Method

- **All or some of the components are combined trough being melted together and cooled with constant stirring until congealed.**

Fusion Method

- Components not to be melted maybe added to the mixture as it is being cooled
- Volatile substances are to be added when the mixture are already at low temperature
- Maybe done in a porcelain dish or beaker
- Beeswax, paraffin and High molecular PEG.
- Must be done according to the boiling point

Preparation of ointments having an Emulsion base

1. Oleaginous bases are melted in a steam bath (70-75 C)
2. At the same time, aqueous solutions are to be heated at the same temperature
3. Slowly add the aqueous solution with constant stirring
4. Cool

Compendial Requirements for Ointments

- **Microbial Content – Preparations with water tend to support microbial growth**
  - **Not required to be sterile**
  - **Examples are Methylparaben, Propylparaben, Phenols, Benzoic Acid, Sorbic Acid and Quarternary Ammonium Salts**

Compendial Requirements for Ointments

- **Must be free from P. aeruginosa, S. aureus, Yeasts and Molds.**
- **Strict compliance to guidelines is required (Testing of raw materials, use of acceptable water and testing of final product)**

Compendial Requirements for Ointments

- **Minimum Fill**
  - **Determination of the net weight or volume of the contents of filled containers to ensure proper contents compared with the labeled amount.**

Compendial Requirements for Ointments

- **Packaging, Storage and Labeling**
  - **Ointments and semisolids are to be place in large mouth ointment jars or metal and plastic tubes.**
  - **To be stored in a cool place and tightly closed container to prevent contamination.**
  - **Labels must include the type of base used**

Compendial Requirements for Ointments

- **Additional Standards**
  - **Viscosity and in vitro drug release**
  - **Diffusion cell studies**
    - **Drug's release from the semisolid product**

Creams

Creams

- **semi-solid dosage preparations containing one or more medicinal agents dissolved or dispersed in either a:**
  - **Water-in-Oil emulsion**
  - **Oil-in-Water emulsion**

Water-in-Oil (cold cream)

Example:

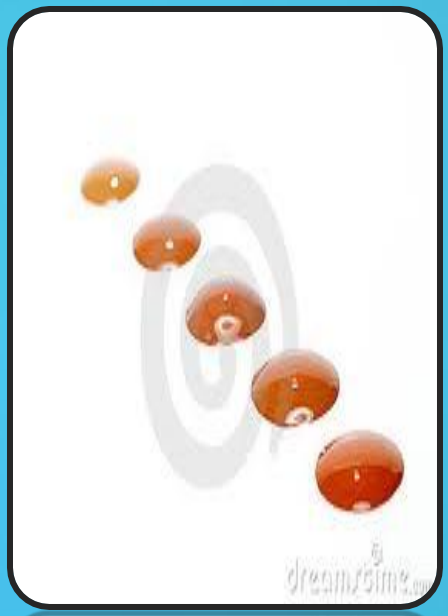
Emollient Cream – Cold Cream (Galen's Cream)

Oil-in-Water (Vanishing Cream)

- **Contains large percentage of water, stearic acid and other oleaginous components**
  - **Example: Shaving cream, Hand cream, foundation cream**
- **Preferred by most physicians and patients because they are easier to SPREAD and REMOVE.**

Oil-in-Water (Vanishing Cream)

Examples:



Gels

Gels

- are semi-solid systems consisting of dispersions of small or large molecules in an aqueous liquid vehicle rendered jellylike by the addition of a gelling agent.
- Sometimes called “Jellies”
- May thicken on standing, forming a “thixorope” and must be shaken before use to liquefy gel and enable pouring.

Examples of Gelling Agents:

- **synthetic macromolecules**

Carbomer 934

Examples of Gelling Agents:

- **Cellulose derivatives**

carboxymethylcellulose

hydroxypropylmethylcellulose

Examples of Gelling Agents:

- **natural gums**

tragacanth

Examples of Gelling Agents:

- **carbomers**

high-molecular-weight water-soluble polymer. They are used as gelling agents at concentrations of 0.5% to 2.0% in water. 910,934,934P,940,941,1342

Types of Gels

single-phase

two-phase

Single-Phase Gels

- **macromolecules are uniformly distributed throughout a liquid with no apparent boundaries.**
  - **Ex: mineral oil combined with polyethylene**

Two-Phase System or Magma Gels

- **mass consisting of floccules of small distinct particles**

Ex:

Milk of Magnesia- consists of a gelatinous precipitate of magnesium hydroxide

To contain a drug substance we use:

- **Solvents: alcohol and propylene glycol**
- **Antimicrobial preservatives: methylparaben, propylparaben and chlorhexidinegluconate**
- **Stabilizers: edetate disodium**

Transdermal Preparations

Transdermal Preparations

- **Designed to deliver a drug systematically**
- **Accomplished by penetrating enhancers: dimethyl sulfoxide, ethanol,propylene glycol, glycerin, PEG,urea, dimethyl acetamide, sodium lauryl sulphate, spans, tweens, lecithin, terpenes, etc…**
- **Commonly compounded: pluroniclechitin**

Transdermal Preparations

Example:

Pastes

- are semisolid preparations intended for application to the skin
- Contain a larger portion of solid material (25%)
- Stiffer than ointments
- Prepared by direct mixing or the use of heat
- Because of the stiffness of paste, they remain in place after application and are employed to absorb serous secretions.

Pastes

- Not suited for application of hairy parts of the body
- Paste still used today: Zinc Oxide paste: 25 % of Zinc oxide, starch and petrolatum. It is better to absorb secretions and protect the skin compared to zinc oxide ointment

Pastes

Examples:

Plasters

- are solid or semi-solid adhesive masses spread on a backing of paper,fabric, moleskin, or plastic.
- Applied to the skin to provide prolonged contact at site.
- Unmedicated plasters provide protection or mechanical support at the site of application

Plasters

- **Medical plasters provide effects at the site of application.**
- **Few used today: salicylic acid plaster used on toes for removal of corns.**

Plasters

Examples:

Glycerogelatins

- are plastic masses containing 15% gelatin, 40% glycerin, 35% water, and 10% added medicinal substances such as zinc oxide.
- Applied to skin for the long term. They are melted before application, cooled to slightly above body temperature and applied to the affected area with a fine brush.

Glycerogelatins

- **Usually covered with a bandage and allowed to remain in place for weeks.**
- **Most recent: Zinc gelatin- used in treatment of varicose ulcers. Also known as zinc oxide boot because of its ability to form a pressure bandage.**

Glycerogelatins

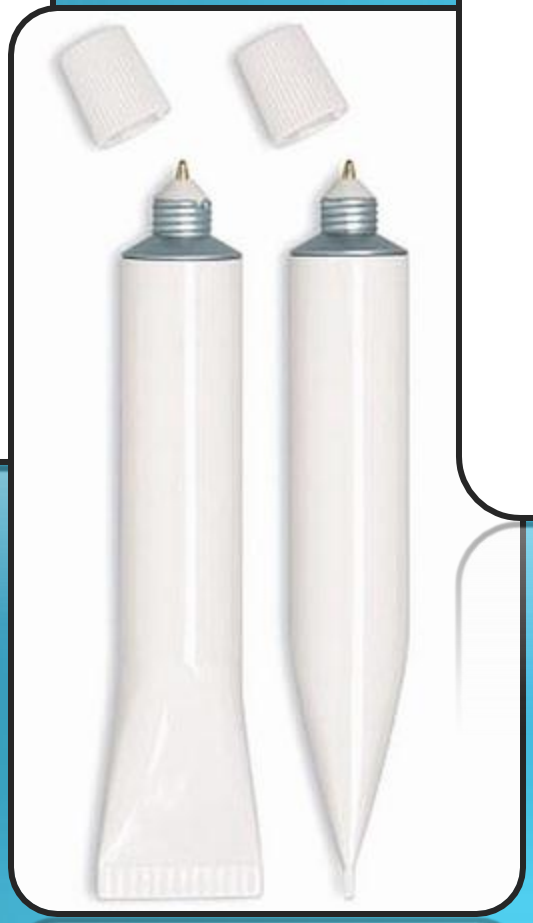
Example:

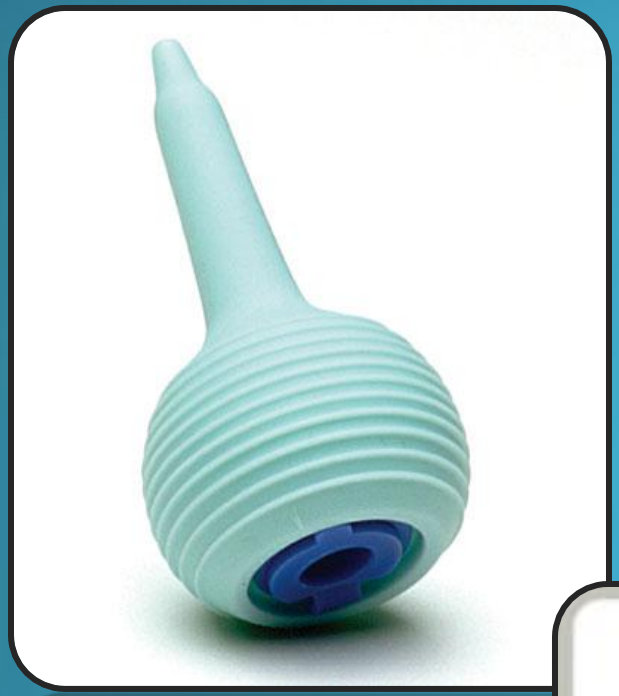
Packaging Semisolid Preparations

Packaging Semisolid Prep.

- **for TOPICAL,**
  - **Jars**
  - **Tubes**
  - **Syringes**

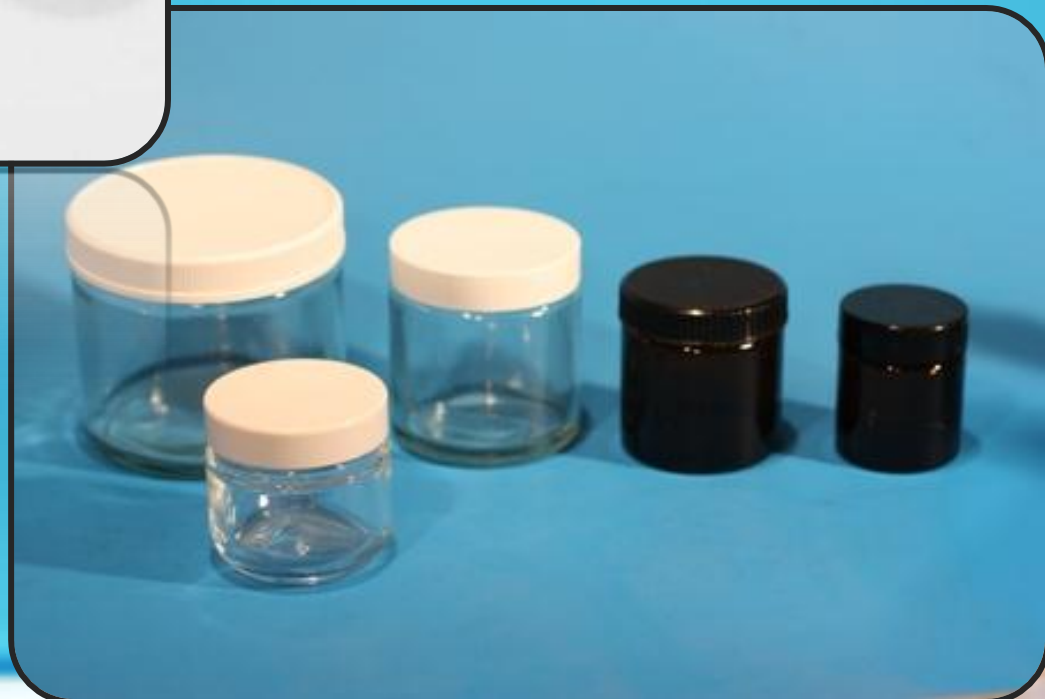
- **for OPTHALMIC, VAGINAL, NASAL AND RECTAL SEMISOLID DF**
  - **Tubes**
  - **Syringes**





Optivisc

JARS



White Plastic Ointment Jars

Case Qty	1/2 oz.	1 oz.	2 oz.	4 oz.	8 oz.	16 oz.
48/case	70050	70001	70002	70004	70008	70016

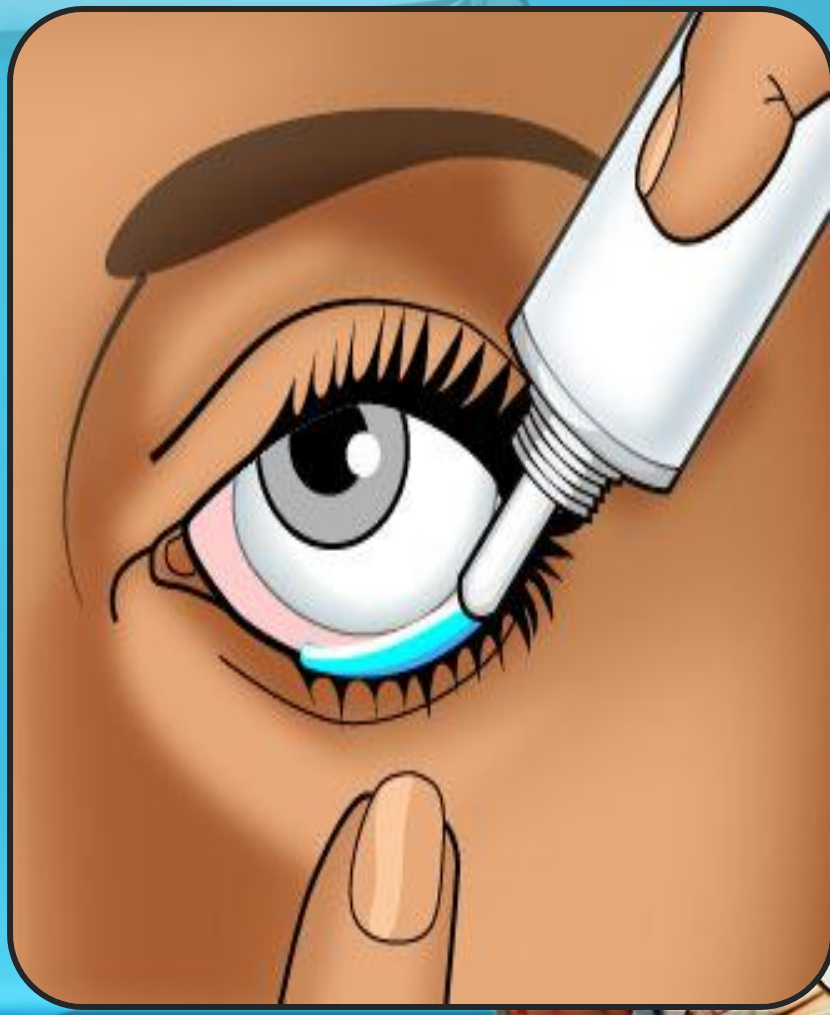
In commercial manufacture and packaging of topical products

- **Compatibility and Stability Test**
  - **Room temperature (20C)**
  - **Accelerated conditions (40C and 50C)**

TUBES

- Light in weight
- Relatively inexpensive
- Convenient for use
- Compatible with most formulative components
- Provide greater protection against external contamination and environmental conditions

boya-pack.www.bizrice.com
BOYA PACKAGING CO.,LTD.



Aluminum tubes

Coated with

- **Epoxy resin**
- **Vinyl**
- **Lacquer**

Plastic tubes

Made of:

- **HDPE or LDPE**
- **PP**
- **PET**
- **Various plastic, foil, paper laminates (10 layers thick**

Plastic tubes

Component	Features and advantages
LDPE (Low-Density Polyethylene)	Soft and resilient Provides good moisture barrier
HDPE (High-Density Polyethylene)	Less resilient Superior moisture barrier
PP (Polypropylene)	High level of heat resistance
PET (Polyethylene Terephthalate)	Offers transparency High degree of product compatibility
Laminates	Provides excellent moisture barrier

TOP
TICO BALM
TRIAMCINOLONA 0,1%
25 g
Crema
冰黄肤乐软膏
아리코트에스
Super
U 4
0-3 HYPO CEMENT

SYRINGES

Advantages:

- **Exclusion of air from the system**
- **Accurate quantities**

Filling Ointment Jars

Filling Ointment Tubes

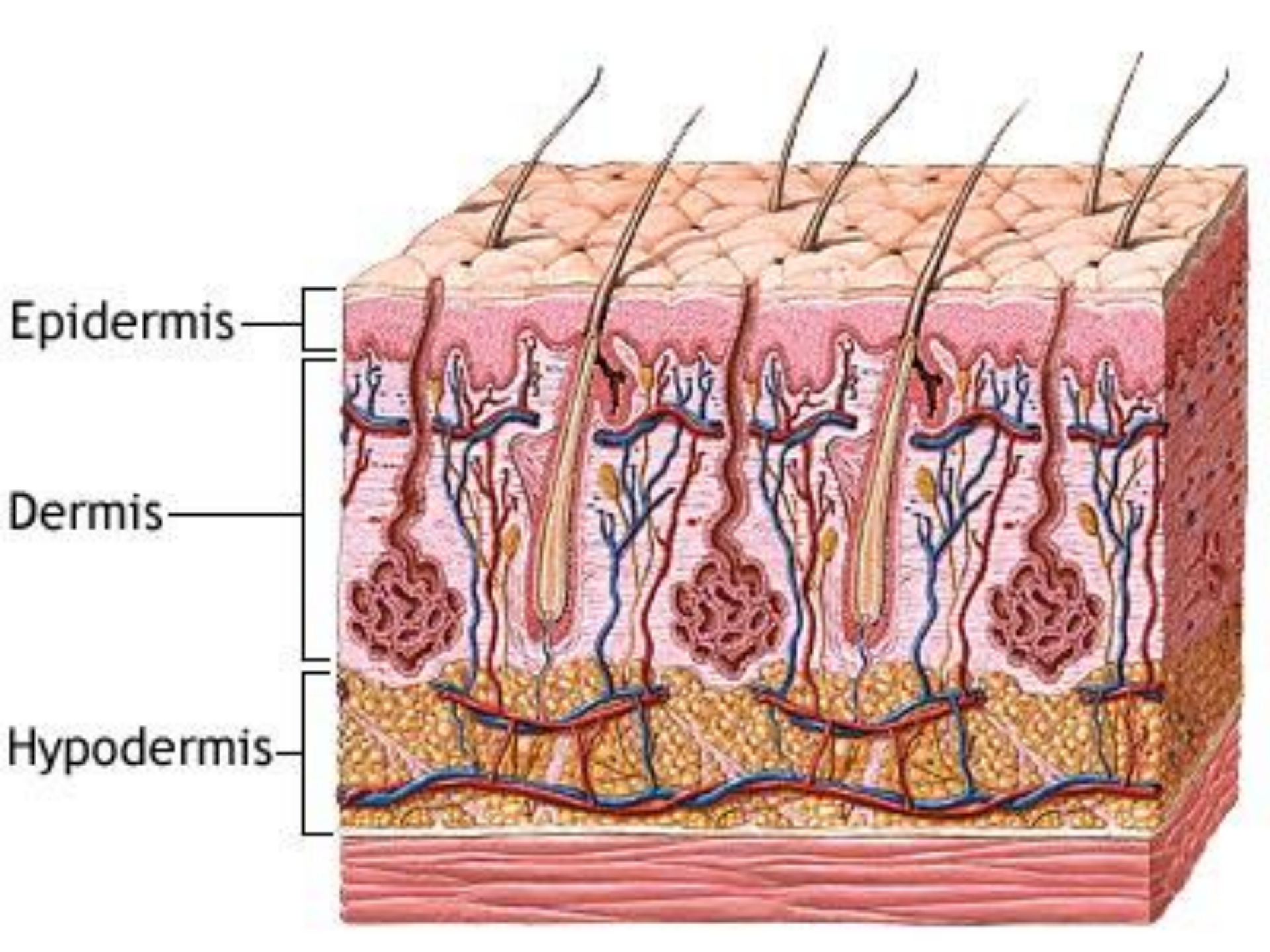
Caulking Gun

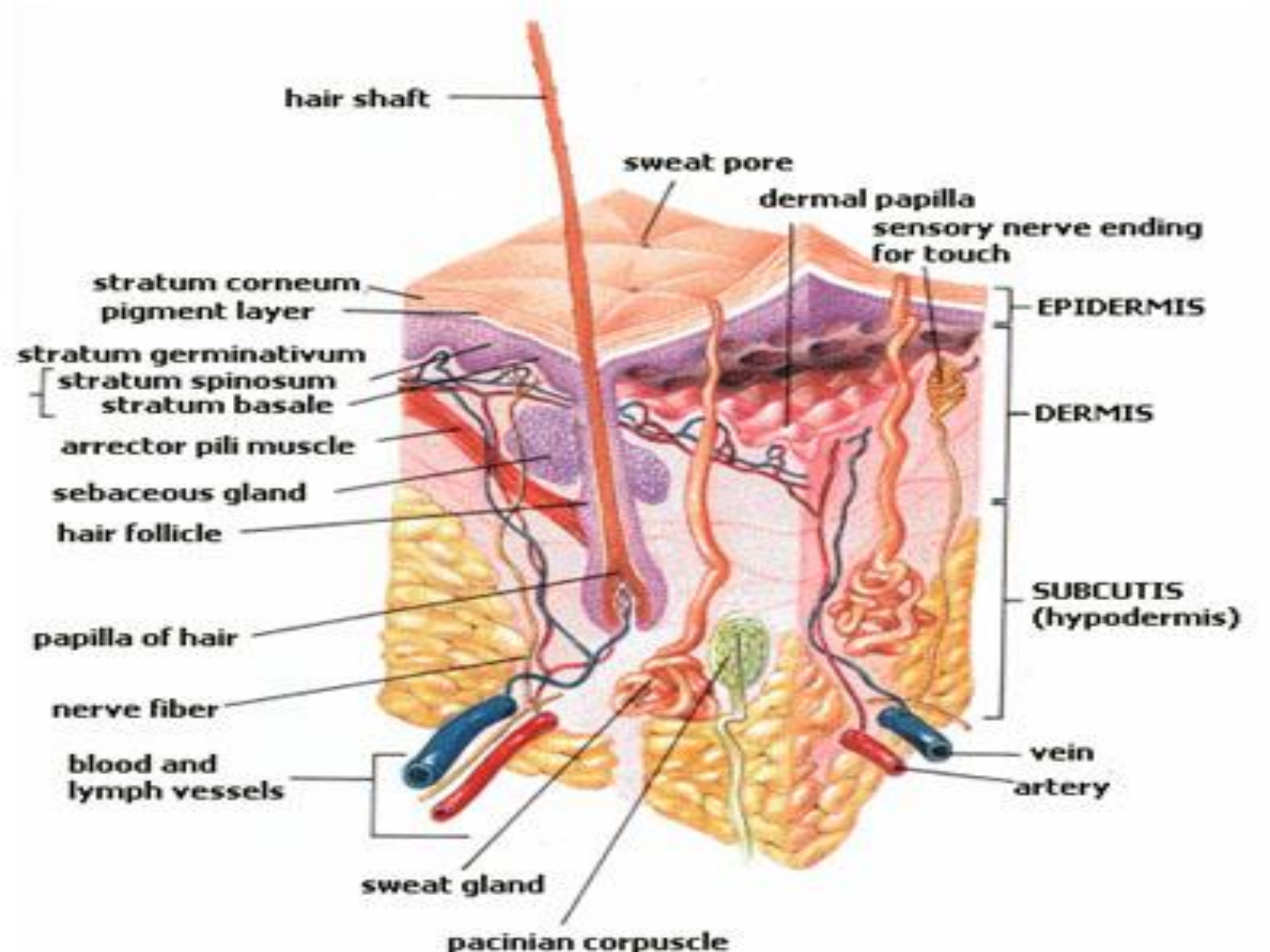
Heat Sealing Crimper

Filling Syringes

Features and Use of Dermatologic Preparations

- in treating skin diseases, the drug in a medicated application ***should penetrate and be retained*** in the skin for a while.
- the stratum corneum functions as a semipermeable artificial membrane and drug penetration is only possible through passive diffusion.
- the rate of drug movement from this skin layer depends on the drug concentration on the vehicle, aqueous solubility and oil-water partition coefficient.
- if the drug reaches the vascularized dermal layer, it becomes available for absorption in the general circulation.


Epidermis
Dermis
Hypodermis


hair shaft
sweat pore
dermal papilla
sensory nerve ending for touch
stratum corneum
pigment layer
EPIDERMIS
stratum germinativum
stratum spinosum
stratum basale
DERMIS
arrector pili muscle
sebaceous gland
hair follicle
SUBCUTIS (hypodermis)
papilla of hair
nerve fiber
vein
blood and lymph vessels
artery
sweat gland
pacinian corpuscle

- Oleaginous bases provide greater occlussion and emollient effects than do hydrophilic and water-washable bases.
- Pastes offer greater occlusion and are more effective than ointments.
- Creams usually o/w emulsions spread more easily than ointments and are easier to remove.
- Water soluble bases are non greasy and easy to remove

- unless directed not to, the patient must thoroughly wash the affected area with soap and water and dried using a soft cloth before applying a dermatologic product.
- typically, 1-3mg of ointment or cream is applied per square cm of the skin.
- unless there is a specified need for an occlusive dressing to protect the area from excessive contact or contaminants, a bandage should not be used.

- upon dispensing the prescription, the pharmacist should be certain that the patient is informed about the proper route of administration, frequence and duration of use, special warning, expected goals and outcomes, signs of adverse effects, allergic reactions, treatment failure and reasons to discontinue treatment and seek health professional guidance.

Examples:

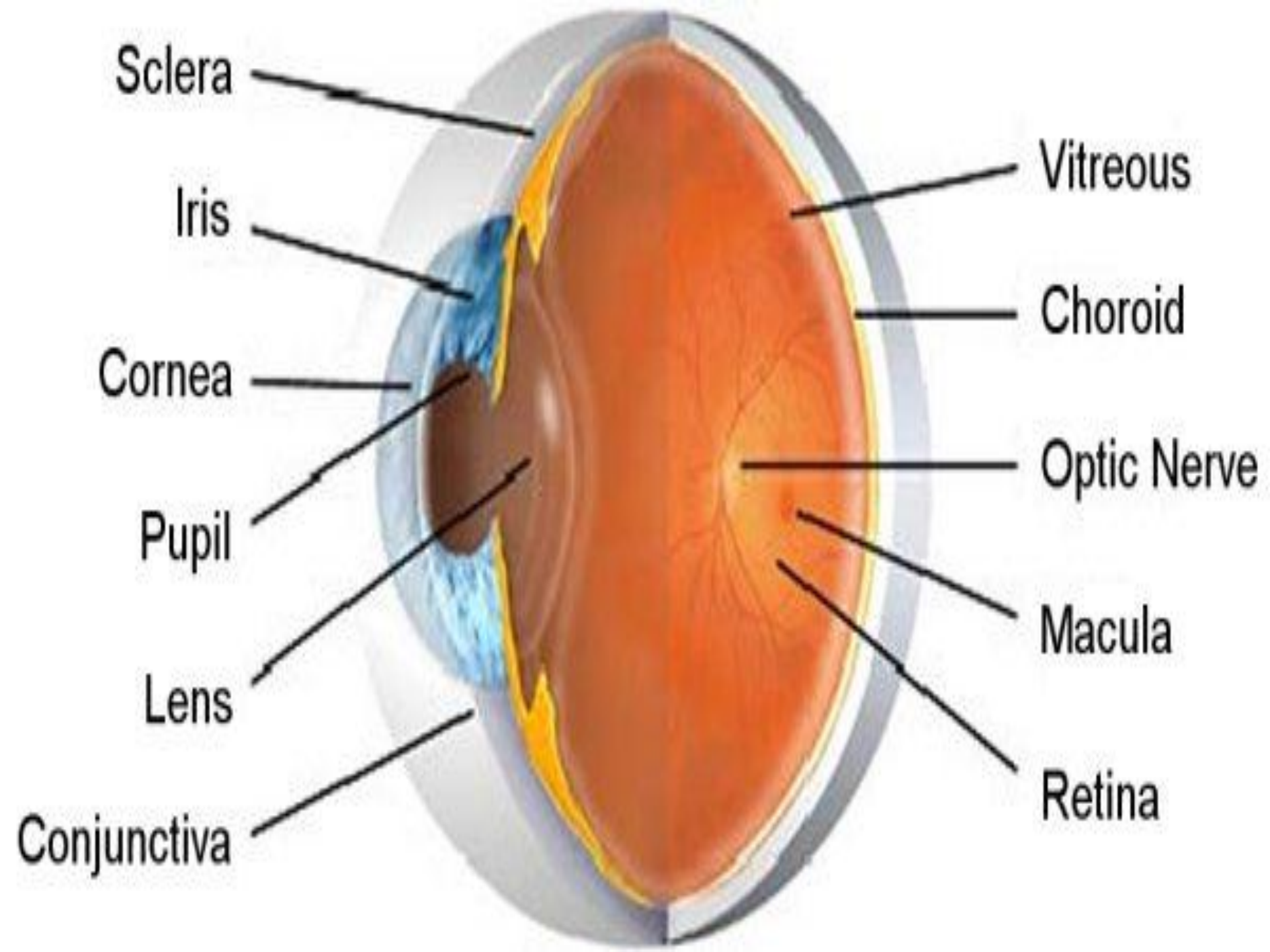
POND'S
age miracle™
Daily Resurfacing Cream
SPF 15 PA++
Advanced CLA* Complex™
POND'S
age miracle

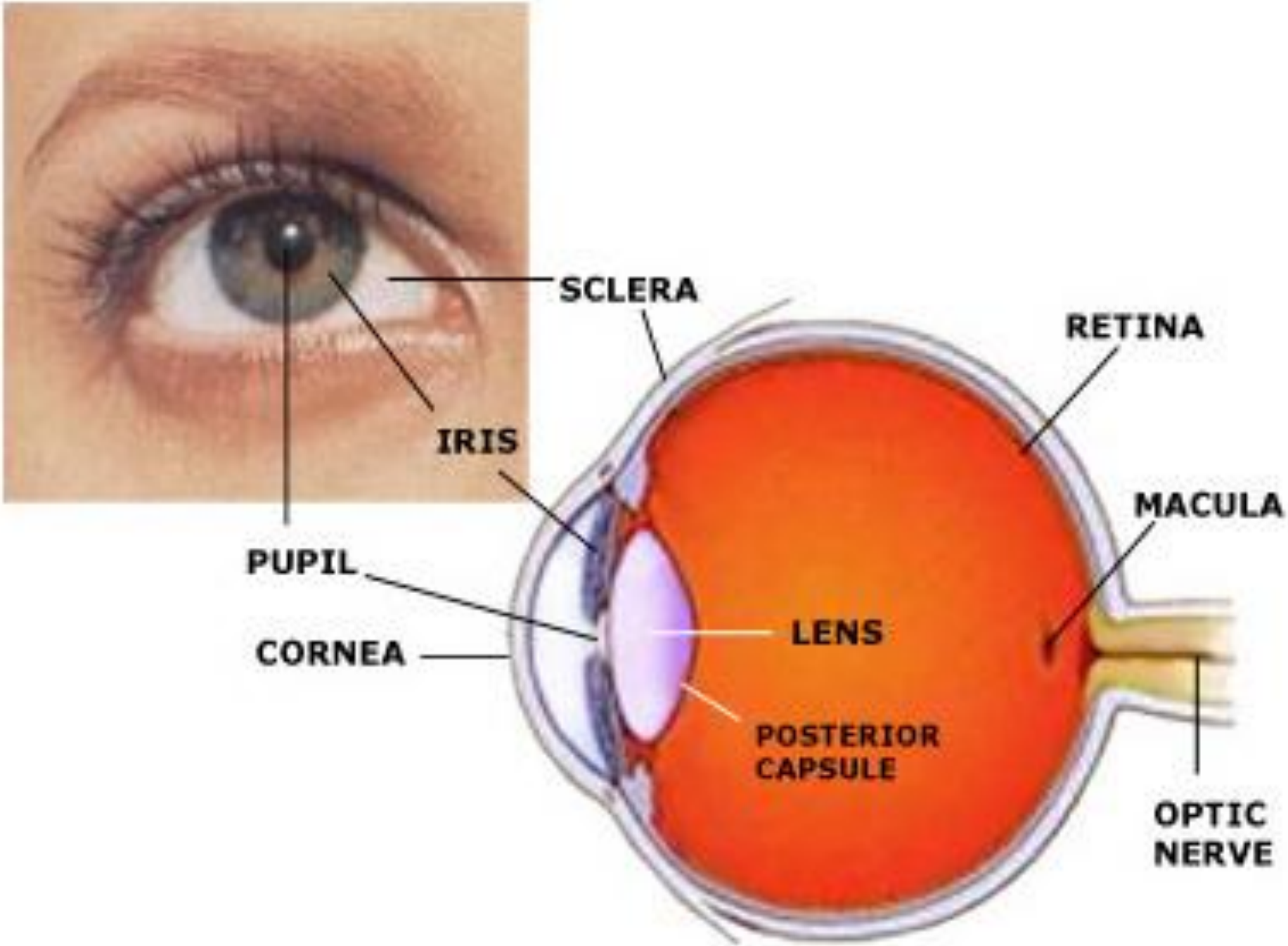
POND'S
dry skin cream
the caring classic
rich hydrating skin cream
Net Wt 10.1 OZ./286g

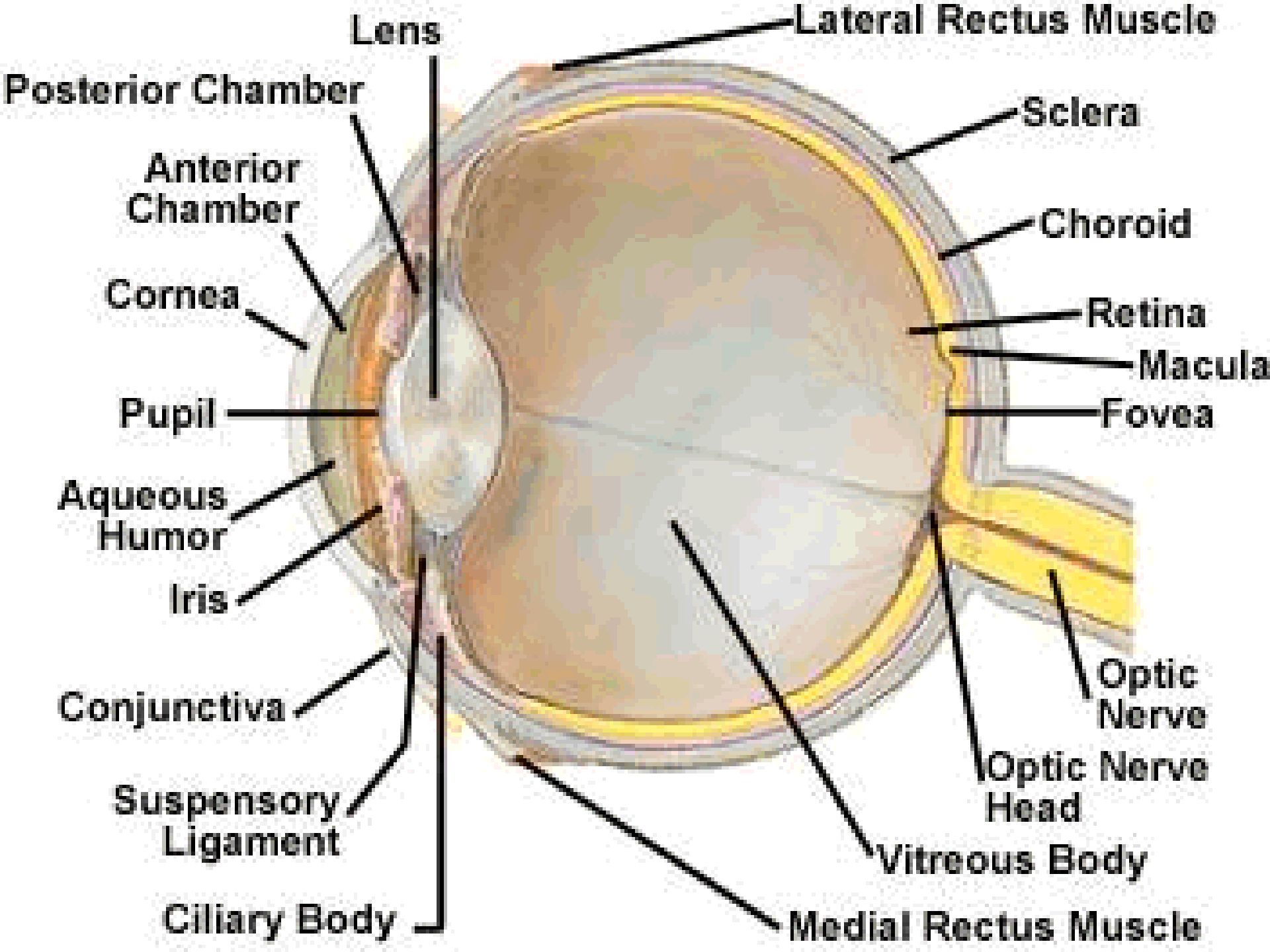
ANEW
ULTIMATE NIGHT
AGE REPAIR CREAM

Features and Use of Opthalmic Ointments and Gels

- the major route by which drugs enter the eye is simple diffusion through the cornea.
- for drugs that are poorly absorbed by the cornea, the conjunctiva and sclera provide an alternate route.


Sclera
Iris
Cornea
Pupil
Lens
Conjunctiva
Vitreous
Choroid
Optic Nerve
Macula
Retina


SCLERA
RETINA
IRIS
MACULA
PUPIL
LENS
CORNEA
POSTERIOR CAPSULE
OPTIC NERVE


Lens
Lateral Rectus Muscle
Posterior Chamber
Sclera
Anterior Chamber
Choroid
Cornea
Retina
Macula
Pupil
Fovea
Aqueous Humor
Iris
Optic Nerve
Conjunctiva
Optic Nerve Head
Suspensory Ligament
Vitreous Body
Ciliary Body
Medial Rectus Muscle

- compared with opthalmic solutions, opthalmic ointments and gels provide extended residence time on the surface of the eye, increasing the duration of their surface effects and bioavailability for absorption to the ocular tissues.
- the ointment base must not cause irritation to the eye and permit the diffusion of medicinal substances troughtout the secretion of the eye

- opthalmic ointments must meet the usp sterility tests and the test for metal particles in opthalmic ointments requirement.
- steam sterilization or ethylene oxide methods are ineffective because netiher is capable of penetrating the ointment base.
- dry heat sterilization can penetrate the ointment base but the high heat might pose a threat to the stability of the drug substance
- because of this, sterilization generally is not undertaken but strict method of asceptic processing are employed.
- antimicrobial preservative – methylparaben & proplylparaben combinations, phenylmercuric acetate, chlorobutanol and benzalkonium chloride.

methylparaben

phenylmercuric acetate

- the usp directs that opthalmic ointments must be packaged in collapsible ointment tubes. these tubes have elongated narrow tip to facilitate a narrow band of ointment to the eye.
- in preparation to apply an ointment to the eye, the patient of caregiver's hand should be washed and dried thoroughly.
- the patient must be advised that blurred vision will occur as the ointment spreads over the eye and not to be alarmed.
- it is important to emphasize that ocular products that are handled improperly can become contaminated by bacteria.

Tears Again
EYE OINTMENT
Mineral Oil and White Petrolatum
Nighttime Relief for Dry Eyes
NET WT. 1/8 fl. oz. (3.5 gm)

Penicillin
OINTMENT
10,000 I. U. PER GRAM
DRUGFIELD
5grams
Penicillin
OPHTHALMIC OINTMENT

Terramycin®
(oxytetracycline hydrochloride)
Antibiotic Ophthalmic Ointment
with Polymyxin B Sulfate
For Animal Use Only
Net Weight 1/8 oz (3.5 g)
Pfizer

Features and Use of Nasal Ointments and Gels

- drugs introduced into the nasal passage are primarily for local effects on the mucous membrane and underlying tissues.
- drug absorption can occur through the blood supply in the nasal lining.
- nasal route holds great promise for the administration of insulin, vaccines, poplypeptides and proteins.

Bactroban Nasal Ointment
mupirocin
3 g

Satisfaction Guaranteed
Made In The USA
MATY'S
Get Better. Do Better.
breathe better
Nasal Ointment
All Natural
Safe For All Ages
Drug Free
Effective Relief
Nighttime Nasal Support
60 DAYS
.5 Oz.

Andaming slides (o.O) pero kulang pa guys. asan yung features of rectal and vaginal use ;) mehehehe.